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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,567	07/22/2003	Sunghoon Kim	012679-093	6562

7590 09/27/2005

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EXAMINER	
LEE, BETTY L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/623,567	KIM, SUNGHOON	
	Examiner	Art Unit	
	Betty Lee, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/08/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/08/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Abstract

The abstract of the disclosure is objected to because at line 8 there are two periods after the term 'thereof' and at line 9 there are extraneous punctuation marks (comma and mark before "re-epithelization") that render the last sentence of the abstract unclear. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claim 9 is objected to because of the following informalities: Claim 9 cites 'the method of claim 6, wherein "said dermatitis" is selected from the group consisting of suburn, chemical burn, radiation burn and thermal burn. The term "dermatitis" lacks antecedent basis in claim 6. Appropriate correction is required.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or

she was in possession of the invention. The invention, for purposes of the written description inquiry, is *whatever is now claimed* (see page 1117).

A review of the language of the claim indicates that these claims are drawn to a genus, i.e., the genus of polypeptides comprising polypeptides having as little as 70% sequence homology with the polypeptide of SEQ ID NO: 1. Since the term "an" is read as encompassing fragments of as few as two amino acids, the claimed genus also encompasses fragments of the polypeptide of SEQ ID NO: 1

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, *i.e. the full length polypeptide of SEQ ID NO: 1*. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described. There is substantial variability among the species. With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides which include variants having as little as 70% sequence identity to SEQ ID NO: 1 and fragments having as few as two amino acids in common with SEQ ID NO: 1. The instant

specification does not disclose any description of fragments or variants of SEQ ID NO: 1. There are no structural and functional features of the claimed genus of polypeptides. There is no description of the conserved regions, which are critical to the structure and function of the genus claimed. Therefore, only the isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 1, but not the full breadth of the claimed genus meets the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

2. Claim 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating wounds by administering the polypeptide of SEQ ID No: 1, does not reasonably provide enablement for methods of treating wounds comprising administering polypeptides with "at least 70% sequence homology" of SEQ ID NO: 1 or for fragments of the polypeptide of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to a method of stimulating wound healing by administering to the subject a composition comprising of the polypeptide of SEQ ID NO: 1, a polypeptide with at least 70% homology with SEQ ID NO: 1, or fragments of the polypeptide of SEQ ID NO: 1.

The state of the prior art and the predictability or lack thereof in the art: The art teaches a high degree of unpredictability that polypeptides having as little as 70% identity with the polypeptide of SEQ ID NO: 1 or fragments of the polypeptide would retain the wound healing function of the full length polypeptide. The art teaches that substitution of even a single amino acid, Lys-145 to Asp will convert the IL-1 receptor antagonist into an antagonist (Ju, *et al* PNAS 88-2658-2662, 1991). The specification does not describe which domains of the polypeptide of SEQ ID NO: 1 convey the function of wound healing. Because the function of a polypeptide correlates with its structure, it would be highly unpredictable whether truncations, substitutions or additions would still render the polypeptide functional.

The amount of direction or guidance present and the presence or absence of working examples: The specification discloses the method of mutating the mouse genomic DNA using a gene trap vector on pg 9, lines 20-26 and pg 10, lines 1-12 and introducing the mutated p43 gene into embryonic stem cells to obtain transgenic mice. However, the specification discloses only one example of a mutated p43 gene (7 kb) and a normal p43 gene (10 kb) of the full length polypeptide of SEQ ID NO: 1 in a Southern gel in Fig 2. The specification has no guidance and no working examples of polypeptides with at least 70% homology to SEQ ID No: 1 which retain wound healing function. Claims 2-9 are dependent on claim 1 and are therefore rejected based on the above reasons.

The breadth of the claims and the quantity of experimentation needed: Because the claims are broadly drawn to methods of treating wounds by administering any of a broadly claimed genus of the fragments and variants of the polypeptides of SEQ ID NO: 1, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kim, *et al* (WO 0195927) in view of Gallucci, *et al* (FASEB J. 14:2525-2531, 2000).

The claimed invention is drawn to a method of stimulating wound healing by administering to the subject a composition comprising of the polypeptide of SEQ ID NO: 1.

Kim, *et al* (WO 0195927) teach the polypeptide p43, which has a 100% homology to SEQ ID NO: 1 of the instant application. Kim, *et al* teach that the p43 protein is a cytokine (see page 1, paragraph 1 and page 2, paragraph 1). Kim, *et al* do not teach a method for stimulating wound healing by administering the polypeptide of SEQ iD NO: 1.

Gallucci, *et al* teach that IL-6, an inflammatory cytokine, promotes wound healing in IL-6 deficient mice. It would have been *prima facie* obvious to use the polypeptide of SEQ ID NO:1 which is a pro-inflammatory cytokine, as taught by Kim, *et al* for treating wounds as suggested by Gallucci, *et al.*

4. Claims 2-5, 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim, *et al* (WO 0195927) in view of Gallucci, *et al* (FASEB J. 14:2525-2531, 2000) as applied to claim 1 supra and further in view of Bennett, *et al* Am. J. Surg 165:728-737, 1993.

The claimed invention is drawn to a method of stimulating wound healing by administering a composition comprising a polypeptide of SEQ ID NO: 1 and one of the group selected from antibiotics, antihistamines, anti-inflammatory drug, anti-viral, anti-fungal drugs and growth factors. The claimed invention is further drawn to a method of treating wounds selected from "burn, ulcer, trauma, post-surgical, post-childbirth,

chronic wound and dermatitis", wherein the composition comprises a pharmaceutically acceptable carrier and is in a formulation selected from cream, lotion, etc.

As was set forth supra, Kim, *et al* teach that the polypeptide of SEQ ID NO: 1 is a cytokine and Gallucci, *et al* teach the administration of cytokines for wound healing. Neither Kim nor Gallucci teach concurrent administration of antibiotics, antihistamines, anti-inflammatory drug, anti-viral, anti-fungal drugs or growth factors.

Bennett, *et al* teach that growth factors like EGF, TGF-β, PDGF, IGF and FGF are involved in wound healing. Moreover, Bennett, *et al* teach that TGF-α and EGF both stimulate mitosis of keratinocytes and fibroblasts and accelerate healing of epidermal injuries (see page 730, col 2). Bennet, *et al* further teach that topical EGF treatment enhances healing of a variety of wounds, including chronic wounds (see page 729, col 1 and 2). Bennett, *et al* teach that FGF stimulate proliferation of most major cell types involved in wound healing including capillary endothelial cells, vascular endothelial cells, fibroblasts, keratinocytes, chondrocytes and myoblasts (see page pg 735, col 2, lines 25-30). Bennett, *et al* teach that EGF treatment heals a variety of wounds including chronic wounds (pg 729, col 2). In addition, Bennett, *et al* teach that both TGF-α and EGF accelerate healing of epidermal injuries (pg 730, col 2).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to treat different types of wounds by administration of the cytokine of SEQ ID NO: 1 in combination with one or more growth factors because Kim, *et al* teach that the polypeptide of SEQ ID NO: 1 is a cytokine, Galluci, *et al* teach that cytokines promote wound healing and Bennett, *et al* teach that also growth factors stimulate and accelerate healing of epidermal injuries.

As set forth in *In re Kerkoven*, 205 USPQ 1069 (CCPA 1980), it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose...the idea of combining them flows logically from their having been individually taught in prior art.

5. Claims 1, 4 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim, *et al* (WO 0195927) in view of Gallucci, *et al* (FASEB J. 14:2525-2531, 2000) and Goddard, *et al* (US Patent 6916648).

Kim, *et al* teach the polypeptide p43, which has a 100% homology to SEQ ID No: 1 of the instant application. Kim, *et al* further teach that the p43 protein is a cytokine. Kim, *et al* do not teach a method for stimulating wound healing by administering p43.

Gallucci, *et al* teach that IL-6, an inflammatory cytokine, promotes wound healing in IL-6 deficient mice.

Goddard, *et al* teach that the growth factor, VEGF is useful for treating diabetic ulcers and vascular injuries resulting from trauma such as subcutaneous wounds in col 47, lines 26-34. Goddard further teaches that the VEGF-E is suitably combined with other ingredients, such as carriers and/or adjuvants and give examples of suitable vehicles including ointments, creams, gels, or suspensions, with or without purified collagen, etc in col 208, lines 6-22.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to combine the polypeptide of Kim, *et al* with a growth factor according to Goddard, *et al* for wound healing. The person of ordinary skill in the art would have been motivated to use growth factors with p43 to stimulate wound healing because Kim, *et al* teach that p43 has cytokine activity, Gallucci, *et al* teach that proinflammatory cytokines are involved in modulating the healing process and Goddard, *et al* teach administration of VEGF for treating wounds.

As set forth in *In re Kerkoven*, 205 USPQ 1069 (CCPA 1980), it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose...the idea of combining them flows logically from their having been individually taught in prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Betty Lee, Ph.D. whose telephone number is (571) 272-8152. The examiner can normally be reached on M-F 9 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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